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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,754	08/29/2005	Nikola Kirilov Kasabov	PEBL-01001US1	6902

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BORSON LAW GROUP, PC
1320 WILLOW PASS ROAD
SUITE 490
CONCORD, CA 94520-5232

EXAMINER

WHALEY, PABLO S

ART UNIT	PAPER NUMBER
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1631

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/524,754	Applicant(s) KASABOV ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request For Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/10/2007 has been entered.

Claims Under Examination

Claims 1-6 and 8-17 are under examination. Claim 7 is cancelled. Claims 8-17 are rejoined in view of applicant's amendments of the claims, which now depend from claims 1 and 3.

Priority

Priority to U.S. Provisional Application No. 60/403,756, filed Aug. 15, 2002, has been acknowledged.

Withdrawn Rejections

The rejection of claims 1-8 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendments, filed 08/03/2007.

The rejection of claims 1-6 under 35 U.S.C. 102 (b) as being unpatentable over Barry et al. (Pat. No. 6,081,786, Issued: Jun. 27, 2000) is withdrawn in view of applicant's amendments and arguments, filed 08/03/2007.

The rejection of claims 1-6 under 35 U.S.C. 102 (b) as being unpatentable over Slonim et al. (Annual Conference on Research in Computational Molecular Biology, Proceedings of the fourth annual international conference on Computational molecular biology, 2000, p. 263 – 272) is withdrawn in view of applicant's amendments and arguments, filed 08/03/2007.

New Matter

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 1 and 5 are now drawn to a system comprising classifier/predictors to classify "to derive" a prediction, and a memory device "to combine predictions derived from classified gene expression information and classified clinical information to predict an outcome of a disease or treatment." Claim 3 is now drawn to a method comprising classifier/predictors "to derive a prediction" and "combining said prediction" from classified clinical and gene expression data to predict an outcome. In the response filed 07/10/2007, applicant does not point to support for the newly recited limitations. These limitations are not taught in the specification and are not present within the scope of the original claims as filed. The specification discloses classifying

array data and clinical data and input this data into a "combined system" which outputs a "predicted outcome" [See Fig. 1 and p.5]. The originally filed claims provide support for prediction of an outcome based on classified gene expression and clinical information data. However, these teachings do not provide support for combining predictions based classified gene expression data and classified clinical data to predict an outcome. As the newly recited limitations are not supported by the originally filed claims or disclosure, the claims are rejected for reciting new matter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. These claims are rejected for the following reasons.

Claims 3 and 13-17 are drawn to a process. Claims 1, 2, 5, 6, and 8-12 are drawn to a system for carrying out a process. For a process to be statutory, it must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), the

statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result. The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to a process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Therefore, for a system that carries out a process to be statutory it must also provide a concrete, tangible, and useful result.

In the instant case, the claimed process does not result in a physical transformation of matter. Where a claimed process does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). Claims 3 and 13-17 result in combining said prediction data to predict an outcome of a disease. This is not a tangible result because the combining of data does not communicate a result in a user readable format. Therefore the claimed method does not recite a practical application of a 35 U.S.C. 101 Judicial exception and is not statutory. Similarly, the system recited in claims 1, 2, 5, 6, and 8-12 results a memory device with software to combine data to predict an outcome of a disease or its treatment. This is not a tangible result because no predicted outcome is communicated in a user readable format. Therefore the claimed product and system do not recite a practical application of a 35 U.S.C. 101 Judicial exception and are not statutory.

This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment. For an updated discussion of statutory

considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Downs et al. (Artificial Intelligence in Medicine, 1996, Vol. 8, p.403-428), in view of Ben-Dor et al. (J Comput. Biol., 2000, Vol. 7, No. 3-4, p. 54-64).

Downs et al. teach a method and system using an adaptive resonance theory based neural network model (ARTMAP), which is broadly interpreted as an evolving fuzzy neural network, for making classifications and predictions of medical data [Abstract]. In particular, Downs shows a fuzzy ARTMAP voting strategy outcome [p.409, Section 3.2] comprising a

number of networks trained on different orderings of the training data; during testing, each individual network makes its prediction for a test item in the normal way; the number of predictions made for each category is then totaled and the one with the highest score (or the most 'votes') is the final predicted category. This voting strategy provides improved performance in comparison to the individual networks. In addition, it also provides an indication of the confidence of a particular prediction, since the larger the voting majority, the more certain is the prediction. The fuzzy ARTMAP consists of 3 modules, 2 fuzzy ART systems, and a related structure called the map field [p.406, ¶3 and Fig. 1] and is applied to training and test data sets. Downs shows the use of clinical and electrocardiographic data considered to be useful for patient prognosis [Section 3.1], as well as the use of tissue samples for predicting breast cancer in patients [Section 4.1, p.411]. Downs also shows employs a 'category pruning' (i.e. decision layer) that functions to improve model specificity based on confidence factors for each classified data cluster, and usage and accuracy scores for each predictive node [Section 4.2.1, p.413]. Downs shows their system can make use of the most highly predictive data (e.g. the ECG codings in the case of myocardial infarction diagnosis) first, and then request additional information on physical signs, associated symptoms, risk factors, clinical history etc (i.e. clinical information) as required, until a confident prediction could be made.

Downs does not specifically teach the use of gene expression data, as in claims 1, 3, 5, and 13.

Ben-Dor et al. teach the use of gene expression data in the development of efficient cancer diagnosis and rule-based classification systems [Abstract]. Ben-Dor show a supervised procedure that can be applied to any parameter independent clustering method [p.56, Col. 2, ¶3] and direct methods for determining a decision surface that are related to artificial neural network applications [Section 2.3, p.56].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Downs as taught above, using gene expression data as taught by Ben-Dor above, resulting in the practice of the instantly claimed invention with predictable results since Downs shows their system can make use of the most highly predictive data first, and then request additional information as required, and can bypass the difficult and time-consuming knowledge-acquisition process found with rule-based expert systems [p.413, ¶1]. One of ordinary skill in the art would have been motivated to combine the above teachings because since gene expression data provide improved insight into cancer related process as shown by Ben-Dor [Abstract].

Claims 1-3, 5, 6, 8-10, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bagne (US 6,317,700; Issued: Nov. 13, 2001), in view of Slonim et al. (Annual Conference on Research in Computational Molecular Biology, Proceedings of the fourth annual international conference on Computational molecular biology, 2000, p. 263 – 272).

Bagne et al. teaches an improved method and system of empirical induction involving longitudinal associations used to evaluate treatments and make predictions. In particular, Bagne presents a computational method of empirical induction (MQALA) that provides high quality predictions about associations between data sets based on generalized conclusions [See Col. 64] and accounts for all characteristics of patients [Col. 68, lines 30-45]. The method of Bagnes uses measured data, applies Boolean features to data to form associations (i.e. first predictions), and computes a longitudinal association score (LAS) for each selected combination of independent events with and dependent events [Ref. Claim 1]. The method is applied to medical and health data wherein the data comprises independent variables that

define treatment events (i.e. first prediction), and dependent variables that are measures of the individual's health (i.e. second prediction), in order to generate an outcome of patient health or health events (i.e. final prediction) [Ref. Claim 19]. Bagnes shows the use of discriminative analysis to identify potential predictors based on demographic characteristics, aspects of patient history, initial values of health measures, assessments of genetic polymorphisms, measures of gene expression, and measures of internal control [Col. 52, lines 55-67], which is suggestive of prediction based on clinical information and gene expression information. Bagnes shows the machines, devices, and software of their system can be in many forms [Section 4.2.6.4] and shows discriminative programs (i.e. modules) and memory [Col. 112, lines 35-50].

Bagne does not specifically teach the use of gene expression data for deriving predictions, as in claims 1, 3, 5, and 13. Slonim et al. teach a method for classifying cancer by computational analysis of gene expression data [Abstract], wherein treatment success (i.e. predicted outcome) predictions are based on a correlation of classified gene expression and chemotherapy data (i.e. classified clinical information) [p.269, Col. 2, ¶ 1], and wherein Bayesian analysis is used for classification, prediction, and confidence testing on all data [p.267, Section 3.3].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Bagne as taught above, using both clinical prediction data and gene expression prediction data as taught by Slonim et al. resulting in the practice of the instantly claimed invention with predictable results, since Slonim discusses research involving classification/predictive methods based on time-course data related to patients and tumors [Introduction]. One of ordinary skill in the art would have been motivated to combine predictions based on gene expression data and clinical data in view of Bagne,

whoshows [Section 2.7.1.2.1 and its 10 subsections] their system allows medical classification systems to account for differences in genomes, gene expression, and measures of internal control that are relevant and important to treatment decisions [Col. 63, ¶4].

Response to Arguments

Applicant's arguments, filed 08/03/2007, that Barry et al. and Slonim et al. do not teach methods for combining independent predictions derived from classified gene expression and clinical data to produce an overall prediction are moot in view of the new grounds of rejections.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Pablo S. Whaley

Patent Examiner
Art Unit 1631
Office: 571-272-4425
Direct Fax: 571-273-4425

/John S. Brusca/
Primary Examiner
Art Unit 1631